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IN THE U.S. PATENT AND TRADEMARK OFFICE

APPLICANT(S):	Kalle SAKSELA *et al.*		
APPLICATION NO.:	09/579,894	GROUP:	1627
FILED:	May 26, 2000	EXAMINER:	B. Celsa
FOR:	METHODS AND MATERIALS FOR GENERATING SH3 DOMAINS WITH TAILORED BINDING PROPERTIES		

DECLARATION SUBMITTED UNDER 37 C.F.R.§1.132

Honorable Commissioner of Patents
Washington, D.C. 20231

I, Dr. Bruce D. Mayer do hereby declare the following.

I am an Associate Professor at the Department of Genetics and Developmental Biology at the University of Conneticut Health Center School of Medicine.

My qualifications as an expert in the field of SH3 domains are in that I was co-author of the first paper describing the isolation of specific SH3 domain binding ligands (Cicchetti *et al.*, Science 1992; 257:803-806), and was co-primary author of the first paper describing the nature of the peptide binding site for SH3 domains (Ren *et al.*, Science 1993; 259:1157-1161). Since that time I have written several reviews in prominent journals on SH3 domains and their binding partners (e.g. Mayer, J. Cell. Sci. 2001; 114:1253-1263). Thus I feel I have appropriate insight into the state of the art in the field at the time of the publication Hiipakka *et al.*, J. Mol. Biol. 1999; 293:1097-1106, disclosing the approach termed as "PRT-SH3

domains", which publication corresponds to the above-identified patent application.

In my view, Dr. Saksela's group's finding in 1999 that it was possible to generate SH3 domains that could bind with high affinity to targeted protein ligands was completely novel and to a large extent unexpected. Although previous work had suggested that it was possible to alter the specificity of an SH3 domain by making specific, directed mutations in the RT loop, this by no means implied that it would be possible to generate SH3 domains with entirely new specificities, not already found in other SH3 domains, by the approach of completely randomizing the RT loop and selecting for high affinity binders to a target of choice. This certainly was not obvious to me at the time, or to anyone else in the field to my knowledge, and represented in my view a major conceptual and practical breakthrough. Furthermore it is only by this "RRT-SH3" approach that one could envision developing SH3 domains that would have potentially useful biological properties as inhibitors or modulators of endogenous signalling pathways.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Bruce W. MAYER, Ph.D.

2/27/04

Date